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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,378	06/23/2003	David Farrow	SMB-004	7906

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SMART AND BIGGAR
438 UNIVERSITY AVENUE
SUITE 1500 BOX 111
TORONTO, ON M5G2K8
CANADA

EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
05/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/601,378	FARROW, DAVID	
	Examiner	Art Unit	
	KARLHEINZ R. SKOWRONEK	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8 and 22-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8 and 22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Interview Summary

Applicant's summary of the interview 14 January 2008 is an accurate reflection of the substance of the interview.

Claim Status

Claims 1-8 and 22-29 are pending.

Claims 9-21 are cancelled.

Claims 1-8 and 22-29 are being examined.

Claim Rejections - 35 USC § 102

Response to Arguments

Applicant's arguments, see Remarks p. 10-11, filed 15 February 2008, with respect to the rejection of claims 1-5, 22, and 26 have been fully considered and are persuasive. The rejection of 1-5, 22, and 26 has been withdrawn in view of the amendments made to the claims.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, see Remarks, p. 12-13, filed 15 February 2008, with respect to the rejection(s) of claim(s) 1-5, 7, 8, and 22-29 under 35 U.S.C. 103(a) as being unpatentable over Tullis et al. in view of Bernhardt et al. and in view of Peterson et al. have been fully considered and are persuasive. Therefore, the rejection has been

withdrawn in view of the amendments made to the claims. However, upon further consideration, a new ground(s) of rejection is made in view of Tullis et al., in view of Bernhardt et al., in view of Peterson et al., and in view of Piesold (IDS entry B1, IDS filed 07 November 2005).

Applicant's arguments, see Remarks, p. 12-13, filed 15 February 2008, with respect to the rejection(s) of claim(s) 1-5, 7, 8, and 22-29 under 35 U.S.C. 103(a) as being unpatentable over Chou et al. in view of Bernhardt et al. have been fully considered and are persuasive. Therefore, the rejection has been withdrawn in view of the amendments made to the claims. However, upon further consideration, a new ground(s) of rejection is made in view of Chou et al., in view of Bernhardt et al., and in view of Piesold (IDS entry B1, IDS filed 07 November 2005).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Amendment of the claims necessitated the following new grounds of rejection.

Claims 1-5, 7, 8, and 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis et al. in view of Bernhardt et al., in view of Peterson et al., and in view of Piesold (WO 01/85341, IDS entry B1, IDS filed 07 November 2005).

The claims are drawn to a method of detecting the presence of an analyte particle, the particle being a virus, specifically Human Immunodeficiency Virus (HIV), in a biological fluid, specifically blood. The method comprises the steps of filtering particulates that are larger than the virus into a first chamber and the virus particulates smaller than the virus in a second chamber, reacting the virus with a reagent to produce a complex that is larger than the virus alone in the second chamber, filtering the virus-reagent complex to remove particles that are smaller from the second chamber, and testing for the presence of the virus in the second chamber. In some embodiments, the reagents is truncated CD4. In some embodiments, filtering is done using injection molded plastic.

Tullis et al. teach a method of filtering HIV from blood using a filter that separates the cells (particles larger than the virus) from the HIV (p. 22, col. 1, para. 3, lines 7-10 to col. 2, line 1). Virus is passed through the filter were it complexes with a ligand reagent (antibodies) reactive to gp120 (p. 22, col. 2, lines 8-11) allow further passage of particles smaller than the viral-reagent complex particles. Tullis et al. teach the detection of Viral-reagent complexes by PCR (col.1, para. 3, lines 10-14).

Tullis et al. does not show Injection molded plastic and a CD4 reagent.

Bernhardt et al. teach the formation of virus-ligand complexes composed of CD4 receptor-HIV (table 1) to result in an increased particle size (col. 2, lines 10-18). The fluid containing the virus-reagent complex is subjected to ultrafiltration thereby allowing particle smaller than the virus-reagent complex to flow through the filter (col. 2, lines 20-29). Bernhardt et al. show that the method will increase the safety of plasma proteins produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration (col. 1, line 10-33).

Piesold describes a microfluidics device having a first chamber and a second chamber used in the filtration of analyte-reagent complexes. Piesold shows the device in figure 2. Piesold shows the device comprises a first chamber “waste”, element 18, and a second “reaction” chamber, element 10. Piesold shows the reagent "beads" in the “reaction” chamber. Piesold shows that the reaction chamber is arranged to correspond in shape to a reaction detection/monitoring means (p. 3, lines 27-28). Piesold shows the device is applied in an example to perform a sequencing-by-synthesis technique in which nucleic acids labeled with biotin are made larger by binding to strepavidin-coated

beads (p. 13, lines 2-12). Although, Piesold shows the use of the device as applied to bead based assays, Piesold suggests that the device is also applicable to assays not involving beads, such as cell-cell separations, cell deformability tests, and particle filtration (p. 2, lines 31-32 to p. 2, lines 1-3). Piesold shows the device provides a reaction apparatus comprising a porous reaction chamber for trapping one or more particles therein and a reaction monitoring means arranged to monitor the particles trapped in the reaction chamber (p. 3, lines 24-28). Piesold shows that the device is shaped to conform to the shape of a reaction chamber-monitoring device (p. 3, lines 14-15). Piesold et al shows the microfluidics device is sealed to allow the optical detection of the chemical reaction in the chamber (p. 12, lines 19-21). Piesold shows in an example a CCD camera is used to collect data from the device (p. 13, lines 20-21). Piesold suggests the device may be used to implement multi-step reactions at a single location (p. 2, lines 18-19). The device of Piesold beneficially enhances the feasibility of miniaturizing many experiments assays, etc.

Peterson et al. show an injection molded plastic filtration device ([0011] and p. 9, claim 1). Peterson et al. teach the device has a solid support for capturing a desired analyte ([0050]). Peterson et al. show that the device has the superior blend of advantages of efficiency and convenience in design manufacture and use ([0010]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the filter device of Tullis with the CD4 reagent of Bernhardt et al. because the binding of HIV to antibodies or to the CD4 protein are functionally equivalent. Bernhardt et al. show in table 1 that antibodies and CD4 are

both suitable reagents for forming a reagent-HIV complex that may be retained during filtration of particle that are smaller than the reagent-virus complex. Bernhardt et al. further motivate one of skill in the art to modify the filter of Tullis et al. because Bernhardt et al. show that the method will increase the safety of plasma proteins produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration. It would have been further obvious to modify the filter of Tullis et al. using the CD4 reagent of Bernhardt et al. with microfluidics device of Piesold because Piesold shows the device provides a beneficial enhancement in the feasibility of miniaturizing experiments and assays. It would have been further obvious to modify the filter of Tullis et al. using the CD4 reagent of Bernhardt et al. with microfluidics device of Piesold because the application of differential filtering was known in the art at the time of invention as demonstrated by Tullis et al and Bernhardt et al. One of ordinary skill in the art would have been capable of applying differential filtering to the device of Piesold that was ready for improvement and the results would have predictable to one of ordinary skill in the art. It would have been further obvious to modify the filter device of Tullis using the CD4 reagent of Bernhardt et al. an the microfluidics device of Piesold with the injection molded plastic filtering device of Peterson et al. because Peterson et al. show that the device has the superior blend of advantages of efficiency and convenience in design manufacture and use.

Amendment of the claims necessitated the following new grounds of rejection.Claims 1-5, 7, 8, and 22-29 rejected under 35 U.S.C. 103(a) as being

unpatentable over Chou et al. (US PGPUB 2004/0072278) in view of Bernhardt et al. (US Pat 6,391,657) and in view of Piesold (WO 01/85341, IDS entry B1, IDS filed 07 November 2005).

The claims are drawn to a method of detecting the presence of an analyte particle, the particle being a virus, specifically Human Immunodeficiency Virus (HIV), in a biological fluid, specifically blood. The method comprises the steps of filtering particulates larger than the virus; reacting the virus with a reagent, producing a complex that is larger than the virus alone; filtering the virus-reagent complex, removing particles that are smaller; and testing for the presence of the virus. In some embodiments, the reagents is truncated CD4. In some embodiments, filtering is done using injection molded plastic.

Chou et al. shows a microfluidics system for particle analysis. Chou shows that viruses are manipulated and analyzed as particles with the microfluidics system ([0167]). Chou et al. shows the microfluidics device has size selective channels that filter particles based on size ([0214]). In an embodiment, Chou et al. shows that blood is filtered with the device ([0460 and 0461]). Chou et al. shows that the device may be configured to have cascaded size selective combs that particles of different sizes are selected ([0468]). This reads on the limitation of the instantly claim invention of filtering out particle larger than the virus and smaller than the virus. Chou et al. teach that the input fluid may be composed of particle of heterogeneous sizes and that device has a size selective retention chambers ([0461]). Chou et al. shows the device is fabricated plastic using a mold ([0127 and 0132]). In example 15, Chou et al. shows that the

microfluidics system is used as a diagnostic tool for analyzing heterogeneous populations of particles based on differences in size ([0655]). In that example, blood is introduced into the device where particles of the fluid are separated and are differentiated based on size. Chou shows that larger particles are retained where smaller particles pass through the size selective barrier ([0660]). Chou shows in example 15 that the particles are treated by exposure to a reagent ([0661]). Chou et al shows the detection of reagent particle complexes. Chou et al. shows the microfluidics system has the advantages of improved speed, accuracy, safety, and cost ([0658]). Chou et al. shows that the CD4 receptor is the primary receptor for the human immunodeficiency virus (HIV) ([0701]).

Chou et al. do not show the formation reagent-particle complex that is separated from particles smaller than the complex or a first chamber and a second reaction chamber separated by a filter.

Bernhardt et al. teach the formation of virus-ligand complexes composed of CD4 receptor-HIV (table 1) to result in an increased particle size (col. 2, lines 10-18). The fluid containing the virus-reagent complex is subjected to ultrafiltration thereby allowing particle smaller than the virus-reagent complex to flow through the filter (col. 2, lines 20-29). Bernhardt et al. show that the method will increase the safety of plasma proteins produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration (col. 1, line 10-33).

Piesold describes a microfluidics device having a first chamber separated from a second chamber by a filter used in the filtration of analyte-reagent complexes. Piesold

shows the device in figure 2. Piesold shows the device comprises a first chamber “waste”, element 18, and a second “reaction” chamber, element 10. Piesold shows the reagent "beads" in the “reaction” chamber. Piesold shows that the reaction chamber is arranged to correspond in shape to a reaction-detection/monitoring means (p. 3, lines 27-28). Piesold shows the device is applied in an example to perform a sequencing-by-synthesis technique in which nucleic acids labeled with biotin are made larger by binding to strepavidin-coated beads (p. 13, lines 2-12). Although, Piesold shows the use of the device as applied to bead based assays, Piesold suggests that the device is also applicable to assays not involving beads, such as cell-cell separations, cell deformability tests, and particle filtration (p. 2, lines 31-32 to p. 2, lines 1-3). Piesold shows the device provides a reaction apparatus comprising a porous reaction chamber for trapping one or more particles therein and a reaction monitoring means arranged to monitor the particles trapped in the reaction chamber (p. 3, lines 24-28). Piesold shows that the device is shaped to conform to the shape of a reaction chamber-monitoring device (p. 3, lines 14-15). Piesold et al shows the microfluidics device is sealed to allow the optical detection of the chemical reaction in the chamber (p. 12, lines 19-21). Piesold shows in an example a CCD camera to collect data from the device (p. 13, lines 20-21). Piesold suggests the device may be used to implement multi-step reactions at a single location (p. 2, lines 18-19). The device of Piesold beneficially enhances the feasibility of miniaturizing many experiments assays, etc.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the differential microfluidics particle filtering system of

Chou et al. with the formation of CD4-HIV complexes for the purpose of increasing the HIV particle size of Bernhardt et al. because Bernhardt et al. show that by forming a reagent-particle complex increased filtration rates can be obtained. It would have been further obvious to use CD4 as the HIV complex-forming reagent because Chou et al. teach that CD4 is the primary receptor for HIV. It would also have been further obvious to modify the filtration device of Bernhardt et al. with the microfluidics system of Chou et al. because Chou et al. teach the microfluidics system has the advantages of improved speed, accuracy, safety, and cost. It would have been further obvious to modify the microfluidics filtering system of Chou et al. using the CD4 reagent of Bernhardt et al. with microfluidics device of Piesold because Piesold shows the device provides a beneficial enhancement in the feasibility of miniaturizing experiments and assays. It would have been further obvious to modify the microfluidics filtering system of Chou et al. using the CD4 reagent of Bernhardt et al. with microfluidics device design of Piesold because the application of differential filtering was known in the art at the time of invention as demonstrated by Bernhardt et al. One of ordinary skill in the art would have been capable of applying differential filtering to the device of Piesold that was ready for improvement and the results would have predictable to one of ordinary skill in the art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

21 May 2008

/K. R. S./
Examiner, Art Unit 1631
/John S. Brusca/
Primary Examiner, Art Unit 1631